EXHIBIT C

Trials@uspto.gov
Tel: 571-272-7822

Paper 18
Entered: August 11, 2021

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

LIQUIDIA TECHNOLOGIES, INC.,
Petitioner,

v.

UNITED THERAPEUTICS CORPORATION,
Patent Owner.

IPR2021-00406
Patent 10,716,793 B2

Before ERICA A. FRANKLIN, CHRISTOPHER M. KAISER, and DAVID COTTA, *Administrative Patent Judges.*

KAISER, *Administrative Patent Judge*.

DECISION
Granting Institution of *Inter Partes* Review
35 U.S.C. § 314

INTRODUCTION

A. Background

Liquidia Technologies, Inc. ("Petitioner") filed a Petition (Paper 2, "Pet.") requesting an *inter partes* review of claims 1–8 of U.S. Patent No. 10,716,793 B2 (Ex. 1001, "the '793 patent"). United Therapeutics Corporation ("Patent Owner") filed a Preliminary Response. Paper 13 ("Prelim. Resp.").

We have authority to determine whether to institute an *inter partes* review. 35 U.S.C. § 314(b) (2018); 37 C.F.R. § 42.4(a) (2020). The standard for instituting an *inter partes* review is set forth in 35 U.S.C. § 314(a), which provides that an *inter partes* review may not be instituted unless "there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition."

After considering the Petition, the Preliminary Response, and the evidence of record, we determine that Petitioner has demonstrated a reasonable likelihood that it would prevail with respect to at least one challenged claim. Accordingly, we institute an *inter partes* review of all challenged claims on all asserted grounds.

B. Related Matters

The parties identify *United Therapeutics Corporation v. Liquidia Technologies, Inc.*, 1:20-cv-00755-RGA (D. Del.) ("the District Court proceeding"), as a related matter. Pet. 1; Paper 3, 1.

C. The Asserted Grounds of Unpatentability

Petitioner contends that claims 1–8 of the '793 patent are unpatentable based on the following grounds (Pet. 30–68):[1]

Claim(s) Challenged	35 U.S.C. §[2]	Reference(s)/Basis
1–8	103	'212 patent,[3] Voswinckel JESC,[4] Voswinckel JAHA[5]
1–8	103	'212 patent, Voswinckel JESC
1	102	Ghofrani[6]
1, 3, 8	103	Voswinckel JAHA, Ghofrani
1, 3	102	Voswinckel 2006[7]

[1] Petitioner also relies on declarations from Nicholas Hill, M.D., and Igor Gonda, Ph.D. Ex. 1002; Ex. 1004.

[2] The '793 patent claims a priority date of May 15, 2006, and Petitioner "assumes the relevant priority date . . . is May 15, 2006." Pet. 12; Ex. 1001, code (60). Accordingly, patentability is governed by the versions of 35 U.S.C. §§ 102 and 103 preceding the amendments in the Leahy-Smith America Invents Act ("AIA"), Pub. L. No. 112–29, 125 Stat. 284 (2011).

[3] US 6,521,212 B1, issued Feb. 18, 2003 (Ex. 1006) (alleged to be prior art under 35 U.S.C. §§ 102(a), (b), (e)).

[4] Voswinckel, R., et al., *Inhaled treprostinil is a potent pulmonary vasodilator in severe pulmonary hypertension*, 25 EUROPEAN HEART J. 22 (2004) (Ex. 1007) (alleged to be prior art under 35 U.S.C. § 102(b)).

[5] Robert Voswinckel, et al., *Inhaled Treprostinil Sodium (TRE) For the Treatment of Pulmonary Hypertension*, in Abstracts from the 2004 Scientific Sessions of the American Heart Association, 110 CIRCULATION III-295 (Oct. 26, 2004) (Ex. 1008) (alleged to be prior art under 35 U.S.C. § 102(b)).

[6] Hossein Ardeschir Ghofrani, et al., *Neue Therapieoptionen in der Behandlung der pulmonalarteriellen Hypertonie*, 30 HERZ 296–302 (June 2005) (Ex. 1010) (alleged to be prior art under 35 U.S.C. § 102(a)). We rely on the English translation that follows the German original article as part of Ex. 1010.

[7] Robert Voswinckel, et al., *Inhaled Treprostinil for Treatment of Chronic Pulmonary Arterial Hypertension*, 144 ANNALS OF INTERNAL MEDICINE

Claim(s) Challenged	35 U.S.C. §[2]	Reference(s)/Basis
2, 4–8	103	Voswinckel 2006, '212 patent

D. The '793 Patent

The '793 patent, titled "Treprostinil Administration by Inhalation," issued on July 21, 2020. Ex. 1001, codes (45), (54). The patent "relates to methods and kits for therapeutic treatment and, more particularly, to therapeutic methods involving administering treprostinil using a metered dose inhaler and related kits." *Id.* at 1:20–23.

Treprostinil "is a prostacyclin analogue" that may be used to treat pulmonary hypertension. *Id.* at 5:37–41. According to the '793 patent, it was previously known to administer treprostinil by intravenous, subcutaneous, or inhalation routes to treat any of several conditions, including pulmonary hypertension. *Id.* at 5:42–58.

The '793 patent relates to the administration of treprostinil in high concentrations over a short inhalation time. *Id.* at 16:61–63, 17:44–46. This method of administration is described as reducing pulmonary vascular resistance and pulmonary artery pressure, as well as increasing cardiac output. *Id.* at 16:32–42, Fig. 10.

E. Illustrative Claim

Claims 1–8 of the '793 patent are challenged. Claim 1 is independent and illustrative; it recites:

> 1. A method of treating pulmonary hypertension comprising administering by inhalation to a human suffering from pulmonary hypertension a therapeutically effective single event dose of a

149–50 (January 2006) (Ex. 1009) (alleged to be prior art under 35 U.S.C. § 102(a)).

> formulation comprising treprostinil or a pharmaceutically acceptable salt thereof with an inhalation device, wherein the therapeutically effective single event dose comprises from 15 micrograms to 90 micrograms of treprostinil or a pharmaceutically acceptable salt thereof delivered in 1 to 3 breaths.

Ex. 1001, 18:23–31.

ANALYSIS

A. Claim Construction

In an *inter partes* review, we construe a claim in an unexpired patent "in accordance with the ordinary and customary meaning of such claim as understood by one of ordinary skill in the art and the prosecution history pertaining to the patent." 37 C.F.R. § 42.100(b) (2020). "[T]he ordinary and customary meaning of a claim term is the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1313 (Fed. Cir. 2005) (en banc). "Importantly, the person of ordinary skill in the art is deemed to read the claim term not only in the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the specification." *Id.*

Neither party presents any terms for construction. Pet. 12–13; Prelim. Resp. 1–56. Accordingly, we determine that no express construction of any claim term is necessary in order to decide whether to institute trial. *Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017) (citing *Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999) ("[O]nly those terms need be construed that are in controversy, and only to the extent necessary to resolve the controversy.")).

B. Discretionary Denial

Patent Owner argues that we should exercise discretion to deny institution, either under 35 U.S.C. § 314(a) or under 35 U.S.C. § 325(d). Prelim. Resp. 9–26. Petitioner disagrees. Pet. 4–11.

1. 35 U.S.C. § 314(a) Discretion

Institution of *inter partes* review is discretionary:

> The Director may not authorize an inter partes review to be instituted unless the Director determines that the information presented in the petition filed under section 311 and any response filed under section 313 shows that there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition.

35 U.S.C. § 314(a). This language provides the Director with discretion to deny institution of a petition. *See Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2140 (2016) ("[T]he agency's decision to deny a petition is a matter committed to the Patent Office's discretion."); Patent Trial and Appeal Board Consolidated Trial Practice Guide ("CTPG") at 55 (November 2019), *available at* https://www.uspto.gov/TrialPracticeGuideConsolidated. The Director has delegated his authority under § 314(a) to the Board. 37 C.F.R. § 42.4(a) ("The Board institutes the trial on behalf of the Director.").

The Leahy-Smith America Invents Act was "designed to establish a more efficient and streamlined patent system that will improve patent quality and limit unnecessary and counterproductive litigation costs." H.R. Rep. No. 112−98, pt. 1, at 40 (2011), 2011 U.S.C.C.A.N. 67, 69 (reviews were meant to be "quick and cost effective alternatives to litigation"); *see also* S. Rep. No. 110−259, at 20 (2008); CTPG 56. The Board recognized these goals, but also "recognize[d] the potential for abuse of the review process by

repeated attacks on patents." *General Plastic Co., Ltd. v. Canon Kabushiki Kaisha*, IPR2016-01357, Paper 19, 16−17 (PTAB Sept. 6, 2017) (precedential).

In *NHK Spring Co., Ltd. v. Intri-Plex Technologies, Inc.*, IPR2018-00752, Paper 8 (PTAB Sept. 12, 2018) (precedential), the Board determined that the advanced state of a parallel proceeding is an additional factor weighing in favor of denying institution under 35 U.S.C. § 314(a). *Id.* at 19–20. In *Apple Inc. v. Fintiv, Inc.*, IPR2020-00019 ("*Fintiv*"), Paper 11, the Board articulated a list of factors that we consider in determining whether to exercise discretion to deny institution based on an advanced stage of a parallel proceeding:

> 1. whether the court granted a stay or evidence exists that one may be granted if a proceeding is instituted;
>
> 2. proximity of the court's trial date to the Board's projected statutory deadline for a final written decision;
>
> 3. investment in the parallel proceeding by the court and the parties;
>
> 4. overlap between issues raised in the petition and in the parallel proceeding;
>
> 5. whether the petitioner and the defendant in the parallel proceeding are the same party; and
>
> 6. other circumstances that impact the Board's exercise of discretion, including the merits.

Fintiv, Paper 11, at 5–6. "These factors relate to whether efficiency, fairness, and the merits support the exercise of authority to deny institution in view of an earlier trial date in the parallel proceeding." *Id.* In evaluating these factors, we take "a holistic view of whether efficiency and integrity of the system are best served by denying or instituting review." *Id.* (citing CTPG 58).

Patent Owner has asserted the '793 patent against Petitioner in the District Court proceeding. Pet. 1; Paper 3, 1. Given the status of the District Court proceeding, Patent Owner argues that we should exercise discretion under *Fintiv* to deny institution. Prelim. Resp. 9–26. We discuss the *Fintiv* factors below.

a. First *Fintiv* Factor: Existence or Likelihood of Stay

Patent Owner contends that this factor weighs in favor of denial. Prelim. Resp. 13–14. Patent Owner contends that Petitioner has not requested a stay of the District Court proceeding, and there is no reason to believe that a stay would be granted if it were requested. *Id.* In support of this assertion, Patent Owner argues that there are patents at issue in the District Court proceeding on which the Board has denied institution of *inter partes* review, leaving the District Court as the only forum in which the invalidity of those patents may be adjudicated. *Id.* Petitioner does not address this *Fintiv* factor. Pet. 4–6.

With regard to the first *Fintiv* factor, Petitioner has not requested a stay of the District Court proceeding, and if such a request is subsequently made, we decline to speculate on the likelihood of a stay being granted. For these reasons, we determine that this factor is neutral.

b. Second *Fintiv* Factor: Proximity of Anticipated Trial Date and Statutory Deadline for Final Written Decision

Patent Owner contends this factor also weighs in favor of denial, because the presently scheduled trial in the District Court proceeding—a three-day trial beginning March 28, 2022—will occur roughly four and a

half months[8] before the projected due date for the Board's Final Written Decision on August 17, 2022. Prelim. Resp. 14–16. Petitioner does not address this factor. Pet. 4–6.

Based on the current trial schedule, there is a relatively high likelihood that the District Court will reach its invalidity determination before we issue our Final Written Decision resolving Petitioner's unpatentability allegations. Thus, we determine that the second *Fintiv* factor weighs in favor of exercising our discretion to deny institution under § 314(a).

c. Third *Fintiv* Factor: Investment in Parallel Proceeding

Under this factor, we first consider Petitioner's timing in filing the Petition. If a petitioner, "faced with the prospect of a looming trial date, waits until the district court trial has progressed significantly before filing a petition," that decision "may impose unfair costs to a patent owner." *Fintiv*, Paper 11, at 11. On the other hand, "[i]f the evidence shows that the petitioner filed the petition expeditiously, such as promptly after becoming aware of the claims being asserted, this fact has weighed against exercising the authority to deny institution." *Id.*

Petitioner asserts that it filed this Petition "within three months of receiving [Patent Owner's] infringement contentions." Pet. 4. Patent Owner argues that this three-month delay "can hardly be referred to as

[8] Patent Owner describes the March 2022 trial as scheduled for "***six months before*** the Board's expected statutory deadline." Prelim. Resp. 15 (emphasis in original). The actual time between the conclusion of the scheduled District Court trial, i.e., March 30, 2022, and the latest date on which the Board's Final Written Decision could be due is four months and 18 days. Accordingly, we analyze this issue based on that anticipated time frame.

'expeditious[]' or 'diligent[].'" Prelim. Resp. 18 (quoting *Fintiv*, Paper 11, 11–12 (alterations in original)). Beyond these bare allegations, neither party explains why the facts here suggest either expeditiousness or lack thereof. Pet. 4; Prelim. Resp. 18. We find no unreasonable delay in Petitioner's filing.

Second, we consider "the amount and type of work already completed in the parallel litigation by the court and the parties at the time of the institution decision." *Fintiv*, Paper 11, at 9. "Specifically, if, at the time of the institution decision, the district court has issued substantive orders related to the patent at issue in the petition, this fact favors denial." *Id.* at 9–10.

Petitioner contends this factor weighs in favor of institution, because "the parties have just begun claim construction proceedings in the district court litigation, have not yet taken any depositions, and have conducted only the initial minimum required discovery." Pet. 5. Patent Owner argues that this factor weighs against institution because "a claim construction hearing is currently scheduled for June 4, 2021," and because "the court [likely] will also enter a Claim Construction Order in the case prior to the Board's decision on institution." Prelim. Resp. 17. In addition, Patent Owner notes that the District Court already has entered an order on a substantive issue, namely an order denying Patent Owner's motion to dismiss Petitioner's invalidity counterclaims due to assignor estoppel. *Id.* (citing Ex. 1014).

Although we appreciate that a *Markman* hearing has been held, we find no evidence in the record that any substantive determinations on validity issues have been made in the District Court proceeding. In some respects, the present circumstances are similar to those in *Sand Revolution*

II, LLC v. Continental Intermodal Group-Trucking LLC, IPR2019-01393, Paper 24 (PTAB June 16, 2020) (informative) (*Sand Revolution*"), in which, as here, the parties exchanged preliminary infringement and invalidity contentions, and the district court conducted a *Markman* hearing. *Id.* at 10. The *Sand Revolution* panel found that, "aside from the district court's *Markman* Order, much of the district court's investment relates to ancillary matters untethered to the validity issue itself" and "much work remains in the district court case as it relates to invalidity: fact discovery is still ongoing, expert reports are not yet due, and substantive motion practice is yet to come." *Id.* at 10–11. One difference between the present case and *Sand Revolution* is that neither party here has directed us to the entry of a *Markman* order by the District Court. In fact, as Patent Owner admits, "the parties to the Delaware Litigation are not disputing any claim terms at issue in the '793 patent," so even the entry of such an order would not materially advance the resolution of any invalidity issue related to the '793 patent. Prelim. Resp. 17. Moreover, here, as in *Sand Revolution*, much work remains to be done in the district court. Fact discovery will continue until September 17, 2021, and dispositive motions will not be filed until November 2, 2021. *Id.* at 11.

On balance, given the timeliness of the Petition and the level of investment of time and resources in the District Court proceeding, coupled with the absence of any substantive determinations on validity issues by the court, we find that this factor weighs against exercising our discretion to deny institution under § 314(a).

d. Fourth *Fintiv* Factor: Overlap Between Issues Raised in Petition and in Parallel Proceeding

Patent Owner contends this factor favors denial of institution, because "[e]ach of the asserted claims in the Delaware Litigation is the subject of this Petition," and especially because both proceedings address claim 1 of the '793 patent, the only independent claim. Prelim. Resp. 21. Patent Owner also argues that this factor favors denial of institution because "[t]hree of the five references in the Petition are also asserted in Liquidia's Preliminary Invalidity Contentions in the Delaware Litigation." *Id.* at 21–22. Petitioner argues that this factor favors institution because three of the eight claims challenged here are not challenged in the District Court proceeding. Pet. 5.

We note first that neither party cites any evidence in support of its allegations regarding overlapping issues. Petitioner states that claims are challenged here that are not challenged in the District Court proceeding but cites no support at all for this position. *Id.* Patent Owner, meanwhile, cites exhibits that provide the dates of service of the parties' preliminary infringement and invalidity contentions but does not direct us to the invalidity contentions themselves. Prelim. Resp. 12 (citing Exs. 2022–2023). In arguing that "[t]here is substantial overlap in the issues relating to the present matter and the Delaware Litigation," Patent Owner cites no sources at all. *Id.* at 21–22. Given the lack of evidence supporting either party's position, we cannot determine whether there is substantial overlap—or, indeed, any overlap at all—between the unpatentability issues raised here and the invalidity issues raised in the District Court proceeding.

If we ignore the lack of evidence and take the parties' allegations at face value, there seems to be at least some overlap between the issues raised here and the issues raised in the District Court proceeding. But, by Patent

Owner's own admission, there are claims challenged here that are not challenged in the parallel litigation, and there are prior-art references asserted here that are not asserted in the District Court proceeding. *Id.* The overlap is, at most, not total, and it may or may not be substantial.

In addition to the arguments regarding the overlap of issues, Petitioner argues that Patent Owner has raised assignor estoppel in the District Court proceeding as a way to block Petitioner's assertion of invalidity, which may preclude Petitioner from litigating these issues in any forum other than before the Board. Pet. 5. In response, Patent Owner stipulates that, if we exercise discretion under § 314(a) to deny institution, Patent Owner will not raise its assignor estoppel arguments in the District Court proceeding. Paper 16, 1–2.

Given the lack of evidence supporting either party's position on the overlap of issues, and given that, even according to the parties' unsupported arguments, there may not be substantial overlap of issues, this stipulation does not affect our analysis of the fourth *Fintiv* factor. There are three possibilities to consider. First, Patent Owner may decline to raise its assignor estoppel arguments. In that case, Petitioner would continue to press whatever invalidity arguments it has raised in the District Court proceeding, but we cannot determine on the present record how substantial the overlap is between those arguments and the unpatentability arguments raised here. Even if the District Court makes its decision before we issue a Final Written Decision, the District Court's decision will not reach every issue that Petitioner raises here. Second, Patent Owner may continue to press its assignor estoppel argument and not prevail, leaving Petitioner free to raise the same invalidity arguments. Again, we cannot determine whether and to

what extent those arguments overlap with Petitioner's unpatentability arguments. Finally, Patent Owner may prevail on its assignor estoppel argument. In that case, Petitioner would be barred from raising any invalidity arguments in the District Court proceeding, and the District Court would then have no opportunity to rule on invalidity, eliminating any overlap with the present proceeding. Patent Owner's stipulation eliminates the possibility that Petitioner will not be able to challenge validity before the District Court, but cannot change the fact that the District Court's decision will not reach every issue that Petitioner raises here.

Thus, we find that there may be some overlap of issues between this proceeding and the District Court proceeding, but this overlap (1) is not total either in terms of claims challenged or in terms of references asserted, and (2) may or may not be substantial. Moreover, if we institute, and thus Patent Owner's stipulation does not take effect, the overlap may disappear altogether, depending on the outcome of Patent Owner's assignor estoppel argument. Accordingly, we find that this factor weighs against exercising discretion to deny institution.

e. Fifth *Fintiv* Factor: Whether Petitioner and Parallel Proceeding Defendant Are Same

The parties do not dispute that the same parties involved in the present proceeding are also involved in the District Court proceeding. Pet. 4–6; Prelim. Resp. 23–24. Thus, this factor weighs in favor of exercising our discretion to deny institution under § 314(a).

f. Sixth *Fintiv* Factor: Other Circumstances (Including Merits)

Patent Owner argues that this factor favors denying institution, because Petitioner "has not set forth 'sufficiently strong' proposed grounds that would support a grant of institution. Prelim. Resp. 24–25. Petitioner argues to the contrary that "the merits of this Petition are strong," both because the Board previously instituted review based on earlier petitions challenging related patents, and because the present Petition asserts a multiplicity of grounds challenging each claim. Pet. 5–6.

We are not persuaded by either party's argument. As discussed below, we determine that Petitioner's case is strong enough to warrant institution of *inter partes* review, contradicting the basis of Patent Owner's argument on this factor. Petitioner's argument that the present petition is unusually strong because the Board previously instituted review on other petitions suffers from multiple defects. First, a petition that presents arguments strong enough to institute review is not necessarily a petition that is so strong as to trigger the sixth *Fintiv* factor. Second, the two petitions on which Petitioner's argument rests both challenged patents other than the '793 patent challenged here. Third, the two petitions in question were filed by parties other than Petitioner. It is at best unclear why the Board's determination to institute review on petitions brought by one party challenging certain claims in certain patents should mandate a determination that the merits of the present Petition, brought by a different party and challenging different claims of different patents, are so strong as to warrant weighing this factor in Petitioner's favor. As for Petitioner's argument that its assertion of multiple grounds to challenge each claim means the Petition is strong, we are not persuaded that the number of asserted grounds of

unpatentability, as opposed to the evidentiary support for and persuasive reasoning behind those grounds, is the proper basis on which to judge the strength of a petition.

Because neither party presents a persuasive argument on the sixth *Fintiv* factor, we find that this factor is neutral with respect to exercising discretion to deny institution.

g. Conclusion

Because the analysis is fact-driven, no single factor is determinative of whether we exercise our discretion to deny institution under 35 U.S.C. § 314(a).

On this record, after weighing all of the factors and taking a holistic view, we determine that the facts in this case that weigh against exercising discretion outweigh the facts that favor exercising discretion. Accordingly, we determine that the circumstances presented weigh against exercising our discretion to deny institution under § 314(a).

2. 35 U.S.C. § 325(d) Discretion

Patent Owner argues that we should exercise our discretion to deny institution under 35 U.S.C. § 325(d). Prelim. Resp. 25–26. Petitioner argues that we should not exercise such discretion. Pet. 6–11.

Section 325(d) provides that the Director may elect not to institute a proceeding if the challenge to the patent is based on matters previously presented to the Office. 35 U.S.C. § 325(d) states, in pertinent part,

> In determining whether to institute or order a proceeding under this chapter, chapter 30, or chapter 31, the Director may take into account whether, and reject the petition or request because, the same or substantially the same prior art or arguments previously were presented to the Office.

In deciding whether to exercise discretion to deny institution under § 325(d), we use a two-part framework, determining first "whether the same or substantially the same art previously was presented to the Office or whether the same or substantially the same arguments previously were presented to the Office," and second, "if either condition of first part of the framework is satisfied, whether the petitioner has demonstrated that the Office erred in a manner material to the patentability of challenged claims." *Advanced Bionics, LLC v. MED-EL Elektromedizinische Geräte GmbH*, IPR2019-01469, Paper 6, at 8 (PTAB Feb. 13, 2020) (precedential) ("*Advanced Bionics*"). To use this framework, we consider the factors set forth in *Becton, Dickinson & Co. v. B. Braun Melsungen AG*, IPR2017-01586, Paper 8, at 17–18 (Dec. 15, 2017) (precedential as to § III.C.5, first paragraph) ("*Becton, Dickinson*"). Specifically, we apply *Becton, Dickinson* factors (a), (b), and (d) to determine whether the same or substantially the same art or arguments previously were presented to the Office, and we apply *Becton, Dickinson* factors (c), (e), and (f) to determine whether Petitioner has demonstrated a material error by the Office. *Advanced Bionics*, at 10. We consider the relevant *Becton, Dickinson* factors below as part of the *Advanced Bionics* framework.

a. *Advanced Bionics* Step One: Same or Substantially the Same Prior Art or Arguments Previously Presented to the Office

In the first step of the *Advanced Bionics* framework, we determine whether the same or substantially the same prior art or arguments presented here previously were presented to the Office. We do so by examining three of the *Becton, Dickinson* factors: "(a) the similarities and material

differences between the asserted art and the prior art involved during examination; (b) the cumulative nature of the asserted art and the prior art evaluated during examination;" and "(d) the extent of the overlap between the arguments made during examination and the manner in which Petitioner relies on the prior art or Patent Owner distinguishes the prior art." *Becton, Dickinson*, at 17–18; *see Advanced Bionics*, at 10.

Here, Petitioner admits that "[t]he art presented in this petition was listed in [Patent Owner's] Information Disclosure Statement." Pet. 7. "Previously presented art includes art . . . provided to the Office by an applicant, such as on an Information Disclosure Statement (IDS), in the prosecution history of the challenged patent." *Advanced Bionics*, at 7–8. Accordingly, all of the art asserted against the '793 patent here previously was presented to the Office.

Given this, we evaluate *Becton, Dickinson* factors (a) and (b) as favoring a finding that the same or substantially the same prior art presented here previously was presented to the Office. The art presented here is not only similar to some art that was before the Office during examination, it is identical, and this identity means that there are no material differences between the art presented here and the art previously before the Office.

b. *Advanced Bionics* Step Two: Material Error by the Office Shown

Because we find that the same or substantially the same prior art presented here previously was presented to the Office, we proceed to the second step of the *Advanced Bionics* framework and determine whether Petitioner has demonstrated a material error by the Office. We do so by examining the three remaining *Becton, Dickinson* factors: "(c) the extent to

which the asserted art was evaluated during examination, including whether the prior art was the basis for rejection;" "(e) whether Petitioner has pointed out sufficiently how the Examiner erred in its evaluation of the asserted prior art; and (f) the extent to which additional evidence and facts presented in the Petition warrant reconsideration of the prior art or arguments." *Becton, Dickinson*, at 17–18; *see Advanced Bionics*, at 10.

With respect to factor (c), Petitioner argues that "no prior art was substantively relied on during examination," because the Office "only issued one substantive rejection during prosecution — for obviousness-type double patenting." Pet. 8 (citing Ex. 1015, 24–28). Patent Owner does not address this factor directly, arguing only that "an analysis of each *Becton* factor is not necessary here." Prelim. Resp. 25–26. On the present record, Petitioner appears to be correct: there was only a single substantive rejection, which did not rely on any of the prior-art references asserted here. Ex. 1015, 1–208. Because the art asserted here was not the basis for a rejection and was not evaluated substantively at all during examination, *Becton, Dickinson* factor (c) weighs in favor of a finding that Petitioner has shown material error by the Office.

With respect to factors (e) and (f), the present Petition argues for the unpatentability of claims 1–8 on six grounds, using multiple combinations of references. As discussed in detail below, we determine that Petitioner has shown at least a reasonable likelihood that it will prevail on its allegation that the challenged claims are unpatentable on at least one of these grounds. In making that determination, we note that several references that were before the Examiner appear on the present record to disclose elements of the challenged claims. For example, Voswinckel JAHA teaches treating

"patients with severe pulmonary hypertension" with "Inhaled Treprostinil Sodium (TRE)" with "3 single breaths" of "TRE solution 600 μg/ml," resulting in "strong pulmonary selective vasodilatory efficacy with a long duration of effect following single acute dosing," and Voswinckel JESC describes "the acute hemodynamic response to inhaled treprostinil" following the administration to patients of nebulized treprostinil solution in concentrations of 16, 32, 48, and 64 μg/ml for 6 minutes, resulting in "significant long-lasting pulmonary vasodilatation" without "adverse effects." Ex. 1008, 3; Ex. 1007, 7.

In addition to showing a reasonable likelihood of prevailing on theories of unpatentability not previously addressed by the Office, Petitioner relies on evidence not previously available, including the declarations from Dr. Hill and Dr. Gonda. Accordingly, *Becton, Dickinson* factors (e) and (f) also weigh in favor of a finding that Petitioner has shown material error by the Office.

c. Conclusion

For the reasons discussed above, we determine that "the same or substantially the same art [asserted here] previously was presented to the Office," but we determine that Petitioner "has demonstrated that the Office erred in a manner material to the patentability of challenged claims." *Advanced Bionics*, at 8. Accordingly, we do not exercise discretion under § 325(d) to deny institution.

C. Asserted Obviousness over '212 Patent, Voswinckel JESC, and Voswinckel JAHA

Petitioner argues that claims 1–8 would have been obvious over the combination of the '212 patent, Voswinckel JESC, and Voswinckel JAHA.

Pet. 30–46. Patent Owner argues that this combination of references fails to teach or suggest all the limitations of any of the challenged claims. Prelim. Resp. 42–55. Patent Owner also argues that Petitioner relies on a reference, Exhibit 1037, that has not been proven to be prior art. *Id.* at 28–32.

1. '212 Patent

The '212 patent teaches "[a] method of delivering benzindene prostaglandins to a patient by inhalation." Ex. 1006, code (57). In particular, the '212 patent teaches the use of "[a] benzindene prostaglandin known as UT-15," which "has unexpectedly superior results when administered by inhalation compared to parenterally administered UT-15 in sheep with induced pulmonary hypertension." *Id.* There is evidence in the present record that "UT-15" was also known as "Remodulin" or "treprostinil sodium." Ex. 1035, 582. According to the '212 patent, the UT-15 may be delivered either as droplets formed "from a solution or liquid containing the active ingredient(s)" via a nebulizer, or as a solid-phase powder via an inhaler. Ex. 1006, 5:30–41.

According to the '212 patent, this method may be used to "treat[] pulmonary hypertension in a mammal." *Id.* at 14:9–12. Moreover, the '212 patent teaches "medical use" of its method in a "human." *Id.* at 7:4–5. The necessary dose to achieve "a particular therapeutic purpose will, of course, depend upon the specific circumstances of the patient being treated and the magnitude of the effect desired by the patient's doctor. Titration to effect may be used to determine proper dosage." *Id.* at 6:66–7:3. "[A]erosolized UT-15 has a greater potency as compared to intravascularly administered UT-15," so the '212 patent teaches delivering "only a fraction (10–50%) of the dosage delivered intravascularly" when using its inhalation delivery

method. *Id.* at 8:8–12. Even at "high doses," however, the '212 patent teaches a lack of "significant non-lung effects, i.e., heart rate, cardiac output." *Id.* at 10:51–54.

2. Voswinckel JESC

Voswinckel JESC discusses a study to investigate "the acute hemodynamic response to inhaled treprostinil." Ex. 1007, 7. Of the 29 patients in the study, eight were administered a placebo, groups of six patients each were administered 16, 32, and 48 µg/mL solutions of treprostinil, and three patients were administered a solution containing 64 µg/mL of treprostinil. *Id.* Each administration used an "OptiNeb ultrasound nebulizer, [made by] Nebu-Tec, Germany" for six minutes. *Id.* For each patient, various measurements were taken before administration of the treprostinil and at 0, 15, 30, 60, 90, 120, 150, and 180 minutes after administration. *Id.* According to Voswinckel JESC, "[t]reprostinil inhalation results in a significant long-lasting pulmonary vasodilatation," and, "at a concentration of 16 µg/mL, near maximal pulmonary vasodilatation is achieved without adverse effects." *Id.*

3. Voswinckel JAHA

Voswinckel JAHA discusses a study of 17 patients with "severe pulmonary hypertension" who received treprostinil inhalations. Ex. 1008, 3. These inhalations each involved "3 single breaths" using a "pulsed OptiNeb® ultrasound nebulizer" and a "600 µg/mL" treprostinil solution. *Id.* In addition, "[t]wo patients with idiopathic PAH received compassionate treatment with 4 inhalations of TRE per day after the acute test" and were "treated for more than 3 months." *Id.* According to Voswinckel JAHA, "inhalation resulted in a sustained, highly pulmonary selective vasodilatation

over 120 minutes," showing "strong pulmonary selective vasodilatory efficacy with a long duration of effect following single acute dosing," and "[t]olerability is excellent even at high drug concentrations and short inhalation times (3 breaths)." *Id.*

4. Reliance on Exhibit 1037

In arguing that claims 1–8 would have been obvious over the combination of the '212 patent, Voswinckel JESC, and Voswinckel JAHA, Petitioner and its declarants cite Exhibit 1037, an English translation of the "Operating Instructions" for the "OPTINEB®-ir Microprocessor Controlled Ultrasonic Nebulizer." Pet. 23; Ex. 1002 ¶ 67; Ex. 1037, 1. Patent Owner argues that Exhibit 1037 is undated and therefore not proven to be prior art, so Petitioner's reliance on it should lead to a determination that Petitioner has not shown a reasonable likelihood of prevailing on this asserted ground. Prelim. Resp. 28–32.

We note first that Patent Owner is correct that Exhibit 1037 bears no date. Ex. 1037, 1–33. Accordingly, Petitioner cannot rely on this exhibit as prior art. But the way Petitioner and its declarants use Exhibit 1037 does not amount to a reliance on it as prior art.

As discussed more fully below, Petitioner and its declarants provide two separate calculations to attempt to establish that the prior art taught or suggested the range of treprostinil doses recited in the challenged claims. Pet. 23, 38–39; Ex. 1002 ¶¶ 65–67, 99–100; Ex. 1004 ¶¶ 56–57. One of these calculations begins with the intravascular dose on the FDA label for Remodulin and adjusts that for the '212 patent's teaching that inhalation requires 10–50% the dose that intravascular administration requires. Pet. 38–39. This calculation does not rely on Exhibit 1037 at all. *Id.*

The other calculation begins with Voswinckel JESC's teaching that patients were administered a nebulized solution over six minutes with a treprostinil concentration of 16, 32, 48, or 64 μg/mL, then multiplies that concentration by the volume of solution that would have been nebulized over a six-minute period. Pet. 23. The evidence supporting that volume of solution comes from Petitioner's declarants. *Id.* (citing Ex. 1002 ¶¶ 65, 67; Ex. 1004 ¶ 56). Dr. Hill testifies that "a [person of ordinary skill in the art] would understand [a six-minute nebulization event] to [deliver] at least 1 mL [of solution]" and that he personally "prescribed volumes of [at] least 1 mL for inhalation therapy using nebulizers." Ex. 1002 ¶ 65. In addition, Dr. Hill also testifies that Exhibit 1037 confirms his understanding of typical nebulization volumes because it teaches "a nebulizing rate of 0.6 mL/min." *Id.* ¶ 67 (citing Ex. 1037, 28). Finally, Dr. Gonda testifies that a person of ordinary skill in the art "would have known in May 2006 that nebulizers conventionally deliver between 1 and 5 mL." Ex. 1004 ¶ 56 (citing Ex. 1029, 11; Ex. 1050, 2; Ex. 1066, 1). Thus, Dr. Hill's testimony regarding his own experience and his opinion of what a person of ordinary skill in the art would have believed about nebulization volumes does not rely on Exhibit 1037. Similarly, Dr. Gonda's testimony regarding his opinion of what a person of ordinary skill in the art would have believed about nebulization volumes does not rely on Exhibit 1037. Only Dr. Hill's separate testimony about confirmation of the knowledge of a person of ordinary skill in the art relies on this exhibit, and in doing so, it relies on Exhibit 1037 not as prior art but merely as evidence of the general knowledge in the art at around the time of the invention. *See Koninklijke Philips N.V. v. Google LLC*, 948 F.3d 1330, 1337–38 (Fed. Cir. 2020)

(PTAB properly relied on general knowledge of skilled artisan supported by expert testimony).

Thus, Petitioner's arguments for the obviousness of the challenged claims rest on calculations that in one case do not rely on Exhibit 1037 and in another case rely on testimony that includes multiple separate sources, of which Exhibit 1037 is only one of at least four. Accordingly, at least on the current record, we are not persuaded that Petitioner improperly relies on Exhibit 1037.

5. Analysis

Petitioner argues that the combination of the '212 patent, Voswinckel JESC, and Voswinckel JAHA teaches or suggests the subject matter of claims 1–8 and that a person of ordinary skill in the art would have had a reason to combine the teachings of these references with a reasonable expectation of success. Pet. 30–46. Patent Owner argues that this combination of references fails to teach or suggest delivering a dose of treprostinil within the dose range of the challenged claims in a single dosing event of one to three breaths. Prelim. Resp. 42–55.

a. Claim 1

(1) "A method of treating pulmonary hypertension comprising administering by inhalation to a human suffering from pulmonary hypertension a therapeutically effective single event dose of a formulation comprising treprostinil or a pharmaceutically acceptable salt thereof"

Claim 1 recites "[a] method of treating pulmonary hypertension comprising administering by inhalation to a human suffering from pulmonary hypertension a therapeutically effective single event dose of a formulation comprising treprostinil or a pharmaceutically acceptable salt

thereof." Ex. 1001, 18:23–27. Petitioner argues that the '212 patent, Voswinckel JESC, and Voswinckel JAHA each teach or suggest this limitation. Pet. 35–37. Patent Owner does not dispute this argument. Prelim. Resp. 42–55.

The '212 patent teaches treating pulmonary hypertension via inhalation of a benzindene prostaglandin called UT-15, which was also known as "treprostinil sodium." Ex. 1006, code (57) (identifying "benzindene prostaglandin" as "UT-15"), 2:66–3:5 ("This invention relates to . . . a method of treating pulmonary hypertension by administering an effective amount of a benzindene prostaglandin to a mammal in need thereof by inhalation."); Ex. 1035, 582 ("UT-15" also known as "treprostinil sodium"). Voswinckel JAHA teaches treating "patients with severe pulmonary hypertension" with "Inhaled Treprostinil Sodium (TRE)" with "3 single breaths" of "TRE solution 600 μg/ml," resulting in "strong pulmonary selective vasodilatory efficacy with a long duration of effect following single acute dosing." Ex. 1008, 3. Voswinckel JESC describes "the acute hemodynamic response to inhaled treprostinil" following the administration to patients of nebulized treprostinil solution in concentrations of 16, 32, 48, and 64 μg/ml for six minutes, resulting in "significant long-lasting pulmonary vasodilatation" without "adverse effects." Ex. 1007, 7.

On the present record, we are not persuaded that the evidence identified by Petitioner shows sufficiently that the '212 patent teaches or suggests the "single event dose" portion of this limitation, but we are persuaded that Voswinckel JAHA and Voswinckel JESC both teach or suggest the first limitation of claim 1. Accordingly, on the present record, Petitioner has shown sufficiently that the combination of the '212 patent,

Voswinckel JESC, and Voswinckel JAHA teaches or suggests this portion of claim 1.

(2) "With an inhalation device"

Next, claim 1 recites "with an inhalation device." Ex. 1001, 18:27–28. Petitioner argues that the '212 patent, Voswinckel JESC, and Voswinckel JAHA each teach or suggest this limitation. Pet. 37. Patent Owner does not dispute this argument. Prelim. Resp. 42–55. The '212 patent teaches the use in its inhalation method of "a nebulizer, inhaler, atomizer or aerosolizer" to "form[] droplets from a solution or liquid containing the active ingredient(s)." Ex. 1006, 5:30–32. Both Voswinckel JESC and Voswinckel JAHA teach the use of a "nebulizer" in their inhalation methods. Ex. 1007, 7 ("OptiNeb ultrasound nebulizer"); Ex. 1008, 3 ("the pulsed OptiNeb® ultrasound nebulizer"). Dr. Hill testifies that a person of ordinary skill in the art would have understood "that nebulizers and inhalers are inhalation devices." Ex. 1002 ¶ 94. Accordingly, on the present record, Petitioner has shown sufficiently that the combination of the '212 patent, Voswinckel JESC, and Voswinckel JAHA teaches or suggests this limitation of claim 1.

(3) "Wherein the therapeutically effective single event dose comprises from 15 micrograms to 90 micrograms of treprostinil or a pharmaceutically acceptable salt thereof"

Claim 1 recites "wherein the therapeutically effective single event dose comprises from 15 micrograms to 90 micrograms of treprostinil or a pharmaceutically acceptable salt thereof." Ex. 1001, 18:28–30. Petitioner argues that the combination of the '212 patent and Voswinckel JESC teaches or suggests this limitation. Pet. 37–40. Patent Owner argues that, given the

teachings of Voswinckel JAHA, a person of ordinary skill in the art would have split the daily dose calculated from the combination of the '212 patent and Voswinckel JESC into four separate single event doses, with none of those individual dosing events delivering a dose within the range recited in claim 1. Prelim. Resp. 49–50.

Petitioner calculates the dose that the prior art teaches delivering by inhalation in two separate ways. First, Petitioner argues that Voswinckel JESC teaches delivering to patients at least one milliliter of a solution containing between 16 and 64 μg of treprostinil per milliliter, resulting in the delivery of between 16 and 64 μg of treprostinil. Pet. 22–24, 38. This calculation relies on the teaching in Voswinckel JESC that "patients inhaled solvent solution (placebo) (n=8) or treprostinil for 6 min (OptiNeb ultrasound nebulizer, Nebu-tec, Germany) in concentrations of 16, 32, 48, and 64 μg/ml (n=6, 6, 6, and 3 patients)." Ex. 1007, 7. It also relies on the testimony of Drs. Hill and Gonda that, over a six-minute nebulization, a person of ordinary skill in the art would have expected the delivery of at least one milliliter of solution. Ex. 1002 ¶¶ 65, 67; Ex. 1004 ¶ 56. Dr. Hill cites as support for his opinion the testimony of Dr. Gonda, as well as his own experience in prescribing inhalation therapy. Ex. 1002 ¶ 65 (citing Ex. 1004 ¶ 56). Dr. Gonda's testimony is supported by his citation to three drug labels showing inhalation doses of between 2.5 and 5 milliliters. Ex. 1004 ¶ 56 n.4. The calculated dose of 16, 32, 48, or 64 μg of treprostinil is within the range of 15–90 μg recited in claim 1.

Patent Owner argues that Petitioner's calculations are for a total daily dose rather than a single event dose. Prelim. Resp. 49–50. With respect to this first calculation, we are not persuaded by Patent Owner's argument on

the present record. It is true, as Patent Owner notes, that Voswinckel JAHA teaches dividing the total daily dose into four separate dosing events. Ex. 1008, 3 ("Two patients with idiopathic PAH received compassionate treatment with 4 inhalations of TRE per day after the acute test," where a single inhalation comprised "3 single breaths, TRE solution 600 µg/ml"). But Petitioner's first calculation is for a single event dose, not a total daily dose. Voswinckel JESC teaches delivering its entire dose—the dose calculated by Petitioner and its declarants as between 16 and 64 µg of treprostinil—over a period of six minutes. Ex. 1007, 7.

On the present record, we determine that Patent Owner is correct that Petitioner's second calculation fails to show a single event dose of between 15 and 90 µg of treprostinil. Petitioner's second calculation relies on the teaching of the '212 patent that the dose of treprostinil delivered by inhalation should be "10–50%" of the dose required for intravascular delivery. Ex. 1006, 8:8–12; *see* Pet. 38–39. Petitioner and Dr. Hill provide calculations of the inhaled dose based on this teaching and the dosing calculations approved by the Food and Drug Administration for intravascular treatment with treprostinil. Pet. 38–39; Ex. 1002 ¶ 100; Ex. 1018, 10. According to those calculations, a person of ordinary skill in the art would have understood that a patient should be treated by inhaling between 10.8 and 58.5 µg of treprostinil, which overlaps the range of 15–90 µg recited in claim 1. Pet. 38–39; Ex. 1002 ¶ 100; Ex. 1018, 10. Importantly, though, these calculations are based on delivering treprostinil intravascularly for 1,440 minutes, or one day, for a total daily dose. Pet. 38–39 (converting a dose of 1.25 ng/kg/min to a total dose by, *inter alia*, multiplying by "(24x60)min"); Ex. 1002 ¶ 100 (same). Although this total

daily dose could in theory be administered once per day, with the entire dose given in a single dosing event, Voswinckel JAHA suggests that it should not be and should instead be broken up into four separate dosing events. Ex. 1008, 3. Even at the high end of the range that emerges from Petitioner's second calculation, one fourth of the total daily dose is less than the fifteen-microgram lower end of the claimed range.

Thus, Voswinckel JAHA teaches splitting the daily dose into four dosing events, and Petitioner does not explain why, despite this teaching, a person of ordinary skill in the art would have split the calculated dose into less than four dosing events. Accordingly, on the present record, we are not persuaded that Petitioner's second calculation shows sufficiently that the combination of the '212 patent, Voswinckel JESC, and Voswinckel JAHA teaches or suggests this limitation of claim 1. As discussed above, however, we are persuaded on the present record that Petitioner's first calculation shows sufficiently that the combination of the '212 patent, Voswinckel JESC, and Voswinckel JAHA teaches or suggests this limitation of claim 1.

(4) "Delivered in 1 to 3 breaths"

Finally, claim 1 recites "delivered in 1 to 3 breaths." Ex. 1001, 18:31. Petitioner argues that Voswinckel JAHA teaches or suggests this limitation. Pet. 40–41. Patent Owner disagrees, arguing that Voswinckel JAHA "does not provide sufficient detail for a person of ordinary skill in the art to determine the precise dosage each patient received." Prelim. Resp. 53–54.

Voswinckel JAHA teaches delivering to patients "a TRE inhalation by use of the pulsed OptiNeb® ultrasound nebulizer (3 single breaths, TRE solution 600 µg/ml)." Ex. 1008, 3. It also reports that "[t]olerability is

excellent even at high drug concentrations and short inhalation times (3 breaths)." *Id.*

Against this evidence, Patent Owner argues that a person of ordinary skill in the art "would not [have been] able to determine the 'single event dose' delivered [in Voswinckel JAHA] without knowing critical details of the pulsed Optineb device." Prelim. Resp. 53 (citing Exs. 2029–2031). Dr. Aaron Waxman, testifying on behalf of Patent Owner, states his opinion that Voswinckel JAHA "does not provide sufficient detail for a person of ordinary skill in the art to determine the precise dosage each patient received," so it "does not teach a therapeutically effective single event dose of 15 micrograms to 90 micrograms." Ex. 2001 ¶ 40.

On the present record, it is unclear why the inability of a person of ordinary skill in the art to determine how much treprostinil was administered in Voswinckel JAHA is important. Petitioner does not rely on Voswinckel JAHA to teach or suggest the delivery of a therapeutically effective dose or the recited dose of fifteen to ninety micrograms; as discussed above, those limitations are taught or suggested by other references. Instead, Petitioner relies on Voswinckel JAHA to teach or suggest only the limitation of claim 1 requiring that the delivery be accomplished in 1 to 3 breaths, which, at least on the present record, Voswinckel JAHA does teach. Accordingly, on the present record, Petitioner has shown sufficiently that the combination of the '212 patent, Voswinckel JESC, and Voswinckel JAHA teaches or suggests this limitation of claim 1.

b. Dependent Claims

Claims 2–8 of the '793 patent depend directly or indirectly from claim 1. Ex. 1001, 18:32–45. Petitioner argues that the combination of the

'212 patent, Voswinckel JESC, and Voswinckel JAHA teaches or suggests the additional limitations of these claims. Pet. 41–46. Patent Owner does not dispute these arguments. Prelim. Resp. 42–55.

We have reviewed the evidence cited by Petitioner with respect to the dependent claims. On the present record, we are persuaded that Petitioner has shown sufficiently that the combination of the '212 patent, Voswinckel JESC, and Voswinckel JAHA teaches or suggests the subject matter of claims 2–8.

c. Reason to Combine

As discussed above, Petitioner has shown sufficiently on the present record that the '212 patent, Voswinckel JESC, and Voswinckel JAHA teaches or suggests every limitation of claims 1–8. This alone is not sufficient to show that the challenged claims would have been obvious; instead, Petitioner also must show that a person of ordinary skill would have had a reason to combine the teachings of the references and would have had a reasonable expectation of success in doing so.

Petitioner argues that a person of ordinary skill in the art would have had a reason to combine the teachings of the '212 patent, Voswinckel JESC, and Voswinckel JAHA. Pet. 30–34. Patent Owner does not dispute this argument. Prelim. Resp. 1–56.

The '212 patent teaches the use of inhaled treprostinil sodium for the treatment of pulmonary hypertension at doses between 10 and 50 percent of the doses needed for intravascular delivery. Ex. 1006, code (57), 6:1–2, 8:8–12. According to the '212 patent, the inhaled treprostinil sodium is used in sheep, which are a model for pulmonary hypertension in humans. *Id.* at 9:14–27. Dr. Hill testifies that, based on these teachings, a person of

ordinary skill in the art would have looked for further information regarding "experimentation [with] inhaled treprostinil in humans." Ex. 1002 ¶ 78. On the present record, such information can be found in Voswinckel JESC, which reports on a study in which humans with pulmonary hypertension inhaled treprostinil and experienced "significant long-lasting pulmonary vasodilatation . . . without adverse effects." Ex. 1007, 7. Thus, the present record shows sufficiently that a person of ordinary skill in the art would have had reason to combine the teachings of the '212 patent with those of Voswinckel JESC.

Dr. Hill testifies that, based on the teachings of these references that treprostinil could safely and effectively treat pulmonary hypertension in humans, a person of ordinary skill in the art "would have motivated to further decrease the 6 minute administration time in Voswinckel JESC." Ex. 1002 ¶ 80. Specifically, Dr. Hill testifies that patients often did not adhere to "inhalation therapy for respiratory diseases," that "[p]oor adherence to medication was known to correlate with worse outcomes," and that "reducing administration time or the number of breaths required for therapy [was known to] improve adherence rates." *Id.* (citing Ex. 1002 ¶¶ 36–37; Ex. 1030, 63; Ex. 1032, 179–80; Ex. 1077, 4). Voswinckel JAHA teaches administering treprostinil in three breaths using a high concentration of treprostinil in the aerosolized solution. Ex. 1008, 3. Accordingly, Dr. Hill testifies that a person of ordinary skill in the art would have looked to Voswinckel JAHA to improve patient adherence to the treatment suggested by the combination of the '212 patent and Voswinckel JESC, providing a reason to combine its teachings with those of the other two references. Ex. 1002 ¶¶ 80–82.

Petitioner argues that a person of ordinary skill in the art would have had a reasonable expectation of success in combining the teachings of these three references because Voswinckel JAHA teaches that "[t]olerability is excellent" for its short-duration, high-concentration treprostinil inhalation therapy. Pet. 33 (citing Ex. 1008, 3). The present record supports this argument. Ex. 1008, 3. In addition, Petitioner notes that other studies "taught safe and effective administration of high dosages of inhaled therapeutics in short durations." Pet. 33–34 (citing Ex. 1010, 298; Ex. 1034, 177). Patent Owner argues that these other studies should not be considered, Prelim. Resp. 54, but even without these studies, the present record shows sufficiently that a person of ordinary skill in the art reasonably would have expected to succeed in combining the teachings of the '212 patent, Voswinckel JESC, and Voswinckel JAHA.

d. Conclusion

On the present record, Petitioner has shown sufficiently that the combination of the '212 patent, Voswinckel JESC, and Voswinckel JAHA teaches or suggests all limitations of claims 1–8 and that a person of ordinary skill in the art would have had a reason to combine the teachings of these references with a reasonable expectation of success. Accordingly, we determine that Petitioner has demonstrated a reasonable likelihood of prevailing on its assertion that claims 1–8 are unpatentable as obvious over the combination of the '212 patent, Voswinckel JESC, and Voswinckel JAHA.

D. Asserted Obviousness over '212 Patent and Voswinckel JESC

Petitioner argues that claims 1–8 would have been obvious over the combination of the '212 patent and Voswinckel JESC. Pet. 46–50. Patent

Owner argues that this combination of references fails to teach or suggest all the limitations of any of the challenged claims. Prelim. Resp. 42–55. Patent Owner also argues that Petitioner relies on a reference, Exhibit 1037, that has not been proven to be prior art. *Id.* at 28–32. This ground and the arguments by both parties differ from the previously discussed ground only in that Petitioner does not rely here on Voswinckel JAHA to teach or suggest any limitation of the challenged claims. *Compare* Pet. 30–46, *with* Pet. 46–50. In particular, Petitioner relies here on routine optimization to reach the limitation of the challenged claims requiring that the single event dose of treprostinil be delivered in one to three breaths. Pet. 47–49.

For the same reasons discussed above, we determine that, on the present record, Petitioner has shown sufficiently that the combination of the '212 patent and Voswinckel JESC teaches or suggests all limitations of claims 1–8, except for the limitation requiring delivery in one to three breaths. Also for the same reasons discussed above, we determine that, on the present record, Petitioner has shown sufficiently that a person of ordinary skill in the art would have had a reason to combine the teachings of these references with a reasonable expectation of success.

Petitioner argues that the combination of the '212 patent and Voswinckel JESC teaches or suggests the final limitation of the challenged claims, delivering inhaled treprostinil treatment in one to three breaths. Pet. 47–49. Specifically, Petitioner argues that the method taught directly by the combination of these references, delivering a single event dose of treprostinil over a six-minute period, would have caused problems with "patient compliance and convenience." *Id.* at 48 (citing Ex. 1002 ¶¶ 128, 130). Petitioner argues further that a person of ordinary skill in the art would have

been motivated to improve patient compliance by reducing the inhalation time, arriving at one to three breaths through routine optimization. *Id.* at 48–49 (citing Ex. 1002 ¶¶ 126–131). The present record supports Petitioner's argument on this limitation.

Dr. Hill testifies that, "[d]ue to known problems with patient adherence . . . a [person of ordinary skill in the art] in 2006 reading the '212 patent and Voswinckel JESC would [have been] motivated to minimize the number of breaths requires for administration of treprostinil by inhalation." Ex. 1002 ¶ 128 (citing Ex. 1002 ¶¶ 36–38). On the present record, the '212 patent itself suggests delivering treprostinil with a discrete number of breaths rather than only via continuous nebulization. Ex. 1002 ¶ 131 (citing Ex. 1002 ¶¶ 116–117) (testifying that delivery of inhaled dry powder requires use of dry-powder inhaler); Ex. 1006, 14:19–21 (claiming delivery of treprostinil as an inhaled dry powder); Ex. 1039, 81 (teaching that dry powder inhalers "are breath-actuated"). Thus, on the present record, Petitioner has shown sufficiently that a person of ordinary skill in the art would have been motivated to modify the combination of the '212 patent and Voswinckel JESC to reduce the delivery time to a discrete number of breaths, with as low a number of breaths as possible.

On the present record, Petitioner has also shown sufficiently that adjustment and optimization of dosing was known. The '212 patent teaches varying "[t]he precise amount" of treprostinil administered "depend[ing] upon the specific circumstances of the patient being treated and the magnitude of effect desired by the patient's doctor." Ex. 1006, 6:56–7:3. Moreover, both Dr. Hill and Dr. Gonda testify that adjustment of dosing for

inhaled therapies was known and common. Ex. 1002 ¶ 130 (citing Ex. 1004 ¶ 35; Ex. 1048, 962); Ex. 1004 ¶ 35 (citing Ex. 1047, 1867; Ex. 1048, 962).

Thus, on the present record, Petitioner has shown sufficiently that the combination of the '212 patent and Voswinckel JESC teaches or suggests delivering inhaled treprostinil treatment in one to three breaths. As discussed above, Petitioner has also shown on the present record that this combination of references teaches or suggests the other limitations of the challenged claims and that a person of ordinary skill in the art would have had reason to combine the teachings of these references with a reasonable expectation of success. Accordingly, we determine that Petitioner has demonstrated a reasonable likelihood of prevailing on its assertion that claims 1–8 are unpatentable as obvious over the combination of the '212 patent and Voswinckel JESC.

E. Grounds Relying on Ghofrani or Voswinckel 2006

Petitioner argues that claim 1 was anticipated by Ghofrani; that claims 1, 3, and 8 would have been obvious over the combination of Voswinckel JAHA and Ghofrani; that claims 1 and 3 were anticipated by Voswinckel 2006; and that claims 2 and 4–8 would have been obvious over the combination of Voswinckel 2006 and the '212 patent. Pet. 50–64. Patent Owner argues that each of these grounds fails because Petitioner fails to show sufficiently that Ghofrani and Voswinckel 2006 qualify as prior art. Prelim. Resp. 32–42. Petitioner disagrees, arguing that these references qualify as prior art under 35 U.S.C. § 102(a). Pet. 25–30.

1. Prior-Art Status of Ghofrani

Ghofrani is an article published in the German journal Herz in June 2005, less than one year before the priority date of the '793 patent.

Pet. 25; Ex. 1010, 9; Ex. 1036 ¶¶ 47–55. Petitioner argues that Ghofrani is prior art to the '793 patent under 35 U.S.C. § 102(a). Pet. 25–27. Patent Owner disagrees, arguing that Petitioner has not shown sufficiently that Ghofrani is "by others" under § 102(a). Prelim. Resp. 32–39.

As both parties acknowledge, establishing prior-art status under § 102(a) requires showing that the reference is "by others," meaning that it was authored by an entity different from the entity that invented the challenged patent. Pet. 26–27; Prelim. Resp. 32–34; *see Lacks Industries, Inc. v. McKechnie Vehicle Components USA, Inc.*, 322 F.3d 1335, 1346 (Fed. Cir. 2003) ("it is well-settled law that an inventor's own disclosure will not anticipate his later invention" unless published more than one year prior to the priority date (internal quotation marks omitted)).

The authors of Ghofrani are "Hossein Ardeschir Ghofrani, Robert Voswinckel, Frank Reichenberger, Friedrich Grimminger, [and] Werner Seeger." Ex. 1010, 9. The inventors of the '793 patent are Horst Olschewski, Robert Roscigno, Lewis J. Rubin, Thomas Schmehl, Werner Seeger, Carl Sterritt, and Robert Voswinckel. Ex. 1001, code (72). Thus, there are, as Petitioner argues, "inventors listed on the '793 Patent that are not listed as authors on Ghofrani, and vice versa." Pet. 26. Specifically, Ghofrani, Reichenberger, and Grimminger authored the Ghofrani reference but were not inventors of the '793 patent; and Olschewski, Roscigno, Rubin, Schmehl, and Sterritt were inventors of the '793 patent but not authors of the Ghofrani reference.

Petitioner argues that these differences alone are sufficient to show that Ghofrani is "by others." *Id.* at 26–27. We agree that it is possible, depending on the state of the rest of the evidence of record, for any

difference between the authors of an alleged prior-art reference and the inventors of a challenged patent to render the reference "by others" for purposes of § 102(a). *See, e.g.*, *In re Katz*, 687 F.2d 450, 455 (CCPA 1982) ("ambiguity [was] created by the printed publication" where authors included people not named as inventors); *cf. In re Land*, 368 F.2d 866, 877 (CCPA 1966) (for purposes of § 102(e), reference authored by one co-inventor was "by another").

That said, it is not necessarily always sufficient for Petitioner merely to show a difference between a list of authors and a list of inventors. Where the record contains evidence that the reference was derived entirely from the work of the inventors or at least one joint inventor, this evidence may be sufficient to show that the reference is not "by others" for purposes of § 102(a). *Katz*, 687 F.2d at 455–56 (finding inventor's declaration of sole inventorship sufficient to render reference authored by inventor and others not "by others"). Although the testimony of an inventor that the reference in question was derived from the inventors' work may be sufficient on its own, at least where it is not "a mere pro forma restatement of the oath in [the inventor's] application," affidavits from the other authors disclaiming the invention are particularly strong evidence that the reference is not "by others." *Id.* ("Submission of such affidavits or declarations would have ended the inquiry . . . ."). Here, the present record appears to contain persuasive evidence that, despite the differences between its list of authors and the list of the inventors of the '793 patent, Ghofrani is not "by others" for purposes of § 102(a).

Petitioner's first argument that Ghofrani is "by others" is that there are people who are authors of Ghofrani who are not inventors of the '793 patent.

Pet. 26. But Dr. Seeger, one of the inventors of the '793 patent, as well as an author of Ghofrani, describes the roles of the other authors of Ghofrani, explaining that Dr. Ghofrani drafted the portion of the article "relating to phosphodiesterase inhibitors," that Drs. Reichenberger and Grimminger drafted the portion of the article relating to "the use of selective endothelin A receptor agonists for treating pulmonary hypertension," and that he and Dr. Voswinckel—another co-inventor—drafted the portion of the article relating to "the use of inhaled iloprost and inhaled treprostinil for treatment of pulmonary hypertension," the only portion on which Petitioner's unpatentability case rests. Ex. 2003 ¶¶ 4–8. Dr. Seeger's testimony is corroborated by the testimony of Drs. Ghofrani, Reichenberger, and Grimminger, each of whom testifies that they "did not make material contributions to" the portion of the Ghofrani reference relating to inhaled treprostinil. Ex. 2004 ¶¶ 4–5; Ex. 2005 ¶¶ 4–5; Ex. 2006 ¶¶ 4–5. This is precisely the type of testimony that the *Katz* court held should "end[] the inquiry" into whether Ghofrani was "by others." 687 F.2d at 455–56. Accordingly, without more and based on the current record, we consider it sufficient to overcome Petitioner's argument that the difference between the Ghofrani authors and the inventors of the '793 patent is sufficient to show that Ghofrani is "by others."

Petitioner also argues that the failure to include some of the inventors of the '793 patent—Olschewski, Roscigno, Rubin, Schmehl, and Sterritt—as authors of Ghofrani renders Ghofrani "by others." Pet. 26–27. But "the fact that a reference does not list any co-inventors as authors . . . is certainly not dispositive in itself." *Allergan, Inc. v. Apotex Inc.*, 754 F.3d 952, 969 (Fed. Cir. 2014); *see* MPEP § 2132.01(I) ("An inventor's or at least one joint

inventor's disclosure of his or her own work within the year before the application filing date cannot be used against the application as prior art under pre-AIA 35 U.S.C. 102(a)."). Moreover, Dr. Seeger explains the roles of the other named inventors in designing trials and clinical studies leading to the patent application. Ex. 2003 ¶¶ 22–27. In particular, Dr. Seeger testifies that the Ghofrani reference did not report on the details of the studies and trials that were in part designed by these other authors, explaining why they did not contribute to writing Ghofrani, even though they were involved in the related work that gave rise to the '793 patent. *Id.* ¶¶ 11–12. Again, then, the evidence presently of record seems to support a determination that Ghofrani is not "by others" for purposes of § 102(a).

On the other hand, we are mindful that the evidence supporting such a determination consists entirely of the testimony of Drs. Seeger, Ghofrani, Reichenberger, and Grimminger, none of whom Petitioner has had an opportunity to depose. *See* Pet. 27. In addition, where a genuine issue of material fact exists due to Patent Owner's submission of testimonial evidence with its Preliminary Response, we will view that issue "in the light most favorable to the petitioner solely for purposes of deciding whether to institute an inter partes review." 37 C.F.R. § 42.108(c) (2020).[9] In light of these two points, we are reluctant to resolve the issue of whether Ghofrani is "by others" in a way that might preclude institution of review. Moreover, as discussed above, we determine that Petitioner has shown a reasonable

[9] This version of Rule 42.108(c) was in effect when the present Petition was filed. Rule 42.108(c) was amended on December 9, 2020, to eliminate the requirement to view such issues in the light most favorable to Petitioner, but only for petitions "filed on or after January 8, 2021." 85 Fed. Reg. 79,120 (Dec. 9, 2020). The present Petition was filed on January 7, 2021. Pet. 69.

likelihood of prevailing with respect to at least one claim on at least one of its grounds, and instituting review on that ground requires institution as to all grounds. *SAS Institute Inc. v. Iancu*, 138 S. Ct. 1348, 1355–56 (2018); *PGS Geophysical AS v. Iancu*, 891 F.3d 1354, 1360 (Fed. Cir. 2018); *AC Techs. S.A. v. Amazon.com, Inc.*, 912 F.3d 1358, 1364 (Fed. Cir. 2019). Accordingly, although we are not persuaded that Petitioner has shown a reasonable likelihood of prevailing as to the grounds that rely on Ghofrani, we institute review on those grounds. To the extent either party disagrees with our interpretation of the law governing whether a reference is "by others," we invite such argument during trial.

2. Prior-Art Status of Voswinckel 2006

The issues and arguments regarding Voswinckel 2006 are quite similar to those discussed above regarding Ghofrani. Petitioner argues that Voswinckel 2006 qualifies as prior art under § 102(a) and that it is "by others" both because some of its authors—specifically, Ghofrani and Grimminger—are not inventors of the '793 patent and because some inventors of the '793 patent—specifically, Olschewski, Roscigno, Rubin, Schmehl, and Sterritt—are not authors of Voswinckel 2006. Pet. 27–30. Patent Owner disagrees, pointing to the testimony of Drs. Seeger, Ghofrani, and Grimminger explaining the role that the other inventors of the '793 patent played, as well as making clear that neither Ghofrani nor Grimminger authored the portion of Voswinckel 2006 that is relevant as prior art. Prelim. Resp. 32–34, 39–42.

For the same reasons discussed above with respect to Ghofrani, we are not persuaded that the current record, without more, establishes that Petitioner has shown sufficiently that Voswinckel 2006 is "by others," but

we institute on the grounds relying on Voswinckel 2006, as we are required to do under *SAS Institute*. To the extent either party disagrees with our interpretation of the law governing whether a reference is "by others," we invite such argument during trial.

CONCLUSION

Upon consideration of the Petition, the Preliminary Response, and the evidence presented, we determine that Petitioner has shown a reasonable likelihood that it will prevail in showing that at least one of the challenged claims is unpatentable. Accordingly, we institute an *inter partes* review of all challenged claims based on all grounds asserted in the Petition.

ORDER

It is hereby

ORDERED that, pursuant to 35 U.S.C. § 314(a), an *inter partes* review is hereby instituted on all claims of the '793 patent and on all relevant grounds set forth in the Petition; and

FURTHER ORDERED that, pursuant to 35 U.S.C. § 314(a) and 37 C.F.R. § 42.4, notice is hereby given of the institution of trial, which shall commence on the entry date of this decision.

For PETITIONER:

Ivor R. Elrifi
Erik B. Milch
Deepa Kannappan
Sanya Sukduang
COOLEY LLP
ielrifi@cooley.com
emilch@cooley.com
dkannappan@cooley.com
ssukduang@cooley.com
zLiquidiaIPR@cooley.com
zpatdocketing@cooley.com

For PATENT OWNER:

Stephen B. Maebius
George Quillin
Jason N. Mock
FOLEY & LARDNER LLP
smaebius@foley.com
gquillin@foley.com
jmock@foley.com

Shaun R. Snader
UNITED THERAPEUTICS CORP.
ssnader@unither.com

Douglas Carsten
April E. Weisbruch
Judy Mohr, Ph.D.
MCDERMOTT WILL & EMERY LLP
dcarsten@mwe.com
aweisbruch@mwe.com
jmohr@mwe.com